Applicant: Susan L. Lindquist et al. Attorney's Docket No.: 17481-003001 / Whitehead Ref. Serial No.: 10/826 157 WHI03-28/MIT Ref. 10256W

Serial No. : 10/826,157 Filed : April 16, 2004 Page : 2 of 6

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

(Currently Amended) A yeast cell comprising two integrated copies of an expression
construct comprising a nucleic acid encoding a protein comprising wild-type human alphasynuclein or mutant human alpha-synuclein A53T-an-alpha-synuclein, wherein the expression
construct is integrated in the genome of the yeast cell, and wherein expression of the nucleic acid
is regulated by an inducible promoter, and wherein such that-induction of production of the
protein is toxic to the yeast cell.

2. (Cancelled)

- 3. (Original) The yeast cell of claim 1, wherein induction of expression of the nucleic acid renders the cell non-viable.
- (Original) The yeast cell of claim 1, wherein induction of expression of the nucleic acid arrests growth of the cell.
 - 5-6. (Cancelled)
- 7. (Original) The yeast cell of claim 1, wherein the yeast is Saccharomyces cerevisiae, Saccharomyces uvae, Saccharomyces kluyveri, Schizosaccharomyces pombe, Kluyveromyces lactis, Hansenula polymorpha, Pichia pastoris, Pichia methanolica, Pichia kluyveri, Yarrowia lipolytica, Candida sp., Candida utilis, Candida cacaoi, Geotrichum sp., or Geotrichum fermentans.

Applicant : Susan L. Lindquist et al. Attorney's Docket No.: 17481-003001 / Whitehead Ref. Serial No.: 10/826,157 WHI03-28/MIT Ref. 10256W

Filed : April 16, 2004

Page : 3 of 6

 (Original) The yeast cell of claim 1, wherein the inducible promoter is GAL1-10. GAL1, GALL, GALS, GPD, ADH, TEF, CYC1, MRP7, MET25, TET, VP16, or VP16-ER.

- 9. (Original) The yeast cell of claim 1, wherein the expression construct is an integrative plasmid.
- 10. (Original) The yeast cell of claim 9, wherein the integrative plasmid is pRS303, pRS304, pRS305, or pRS306.
- 11. (Original) The yeast cell of claim 1, wherein the protein is a fusion protein comprising a detectable protein.
- 12. (Original) The yeast cell of claim 11, wherein the detectable protein is a fluorescent protein, an enzyme, or an epitope.
- 13. (Original) The yeast cell of claim 12, wherein the detectable protein is a fluorescent protein selected from the group consisting of a red fluorescent protein, green fluorescent protein, blue fluorescent protein, yellow fluorescent protein, and cyan fluorescent protein.
- 14. (Original) The yeast cell of claim 1, wherein at least one gene that encodes a polypeptide involved in drug efflux or cell permeability is disrupted.
- 15. (Original) The yeast cell of claim 14, wherein the at least one gene is PDR1, PDR3, or ERG6.
 - (Original) The yeast cell of claim 14, wherein the at least one gene is PDR5.
- 17. (Currently Amended) A yeast cell comprising two integrated copies of an expression construct comprising a nucleic acid encoding a protein comprising wild-type human alpha-

Applicant : Susan L. Lindquist et al. Attorney's Docket No.: 17481-003001 / Whitehead Ref. Serial No.: 10/826,157 WHI03-28/MIT Ref. 10256W

Filed : April 16, 2004
Page : 4 of 6

synuclein or mutant human alpha-synuclein A53T, wherein the cell expresses expressing a toxicity-inducing amount of the a protein-comprising an alpha synuclein.

18-21. (Cancelled)

- 22. (Original) The yeast cell of claim 17, wherein the yeast is Saccharomyces cerevisiae, Saccharomyces uvae, Saccharomyces kluyveri, Schizosaccharomyces pombe, Kluyveromyces lactis, Hansenula polymorpha, Pichia pastoris, Pichia methanolica, Pichia kluyveri, Yarrowia lipolytica, Candida sp., Candida utilis, Candida cacaoi, Geotrichum sp., or Geotrichum fermentans.
- (Withdrawn) A method of identifying a compound that prevents or suppresses alpha-synuclein-induced toxicity, the method comprising:

culturing the yeast cell of claim 1 in the presence of a candidate agent and under conditions that allow for expression of the protein at a level that, in the absence of the candidate agent, is sufficient to induce toxicity in the yeast cell; and

determining whether toxicity in the yeast cell is less in the presence of the candidate agent as compared to in the absence of the candidate agent,

wherein if the toxicity is less in the presence of the candidate agent, then the candidate agent is identified as a compound that prevents or suppresses alpha-synuclein-induced toxicity.

24-26. (Cancelled)

 (Withdrawn) A method of identifying an extragenic suppressor of alpha-synucleininduced toxicity, the method comprising:

culturing the yeast cell of claim 1, wherein an endogenous gene of the yeast cell has been disrupted, under conditions that allow for expression of the protein at a level that, in the absence of the disruption of the endogenous gene, is sufficient to induce toxicity in the yeast cell; and

determining whether toxicity in the yeast cell is less in the presence of the disruption of the endogenous gene as compared to in the absence of the disruption of the endogenous gene, Applicant: Susan L. Lindquist et al. Attorney's Docket No.: 17481-003001 / Whitehead Ref. Serial No.: 10/826,157 WHI03-28/MIT Ref. 10256W

Filed : April 16, 2004 : 5 of 6

Page

wherein if the toxicity is less in the presence of the disruption of the endogenous gene, then the disrupted endogenous gene is identified as an extragenic suppressor of alpha-synucleininduced toxicity.

28-42. (Cancelled).